Cortical activation during foot movements: II Effect of movement rate and side

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Cerebral control of foot movements has received limited study. Functional MRI compared slow with rapid foot movement, and right (dominant) with left foot movement. Brain activation during right, as compared with left, foot movement was larger, with higher amplitude task-related motor cortex signal change, and higher laterality index. Brain activation during fast, as compared with slow, foot movement was larger in cortical and cerebellar areas but smaller in deep gray areas. Some principles of cerebral control of hand movement extend to foot, but exceptions found include that dominant foot movement showed greater activation than did nondominant, and faster foot movements activated bilateral deep gray matter structures less than did slower. Results might have utility in trials of restorative therapies. *NeuroReport* 19:1573–1577

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Introduction

Movement of the foot at the ankle, such as occurs during gait, is among the more common movements made by humans and is thus a central component of many physical and social behaviors. Abnormalities of foot movement are a common sequela of many neurological conditions. Despite appreciation of the importance of central nervous system motor structures to the control of foot movements [1,2], however, few studies to date have examined cerebral control of foot movements in humans.

Some topics related to cerebral control of foot movements that have been studied include somatotopy [3,4], movement amplitude [5], and movement guidance/feedback [6]. One recent study described unique profiles of brain activation distinguishing executed, imagined, and observed foot movements [7]. This current study evaluated two additional motor control parameters, foot movement side and rate, which have been examined previously for hand movements. Regarding movement side, left, as compared with right, hand movement has generally been associated with primary sensorimotor cortex (SMC) activation that is larger and more bilaterally organized [8–11]. Regarding movement speed, faster right hand movement is associated with increased activation within multiple areas, particularly contralateral SMC, supplementary motor area (SMA), and ipsilateral cerebellum [11–13].

This current study used functional MRI (fMRI) to examine these two motor control issues, each in a separate cohort of healthy right-handed participants, in relation to foot movements. Right and left foot movement were characterized then contrasted. Next, slow and fast right foot movements were similarly analyzed. The main hypotheses examined were that changes in these foot movement variables would influence brain activity in a manner similar to what has been described for hand movement.

Methods

Participants

For the two fMRI studies as well as the electromyography (EMG) study, entry criteria were age 18–80 years, right-handed on the Edinburgh inventory [14], and right-footed on the Coren footedness inventory [15]. Scores for handedness and footedness with these scales range from +2 (right dominant) to –2 (left dominant). Exclusion criteria were: (i) major neurological or psychiatric disease, (ii) pregnant or lactating, and (iii) contraindication to MRI scanning. Participants signed consent in accordance with local Institutional Review Boards.

MRI acquisition

Participants were positioned in the scanner (Philips, Best, The Netherlands, 1.5T) with knees mildly flexed atop a pillow, and bilateral splints placed. These MRI-compatible ankle splints went from lower tibia to toes, and restricted ankle movement to 10 degrees of ankle dorsiflexion/plantarflexion and prevented lateral leg rotation. Scanning began with a T1-weighted, high-resolution (1 mm^3 voxels)

volumetric anatomical scan covering the entire brain, which was followed by two fMRI scans.

For the movement rate study, the first fMRI task was slow movement, consisting of 30 seconds of rest alternating with 30 s of 0.25 Hz right ankle dorsiflexion/plantarflexion movement, that is, 10 degrees ankle dorsiflexion then 10 degrees ankle plantarflexion every 4 s. The second task was the fast movement task, in which rest alternated with right ankle dorsiflexion/plantarflexion movement at a self-defined maximum rate. Scanning parameters were 25 axial slices, 4 mm thick with a 1-mm interslice gap, repetition time equals 2500 ms, echo time equals 40 ms, 110 volumes over 4 min 35 s, for each of the two tasks.

For the movement side study, the first task was right foot movement, consisting of 30 s of rest alternating with 30 s of 0.33 Hz right ankle dorsiflexion/plantarflexion movement, that is, 10 degrees ankle dorsiflexion then 10 degrees ankle plantarflexion every 3 s. The second task was left foot movement, which consisted of 30 s of rest alternating with 30 s of 0.33 Hz left ankle dorsiflexion/plantarflexion movement. Scanning parameters were 28 axial slices, 4 mm thick with a 1-mm interslice gap, repetition time equals 3000 ms, echo time equals 40 ms, 170 volumes over 8 min 30 s, for each of the two tasks.

Except for the fast movement task, movement rates were guided by a visual metronome present during all blocks, flashing green at desired movement rates and flashing red during rest blocks. For the fast movement task, the same visual stimulus was presented as for the slow task but instructions were changed such that the green flash indicated moves as fast as possible. Participant's behavioral performances during fMRI scanning were recorded by a study investigator.

Electromyography assessments

In a separate cohort of 10 participants, surface EMG was collected while the participant rehearsed both fMRI tasks. With the participant supine, bipolar surface EMG leads were affixed to right tibialis anterior (TA) and to left TA. While EMG was recorded at 2000 samples/s, participants followed the same cues presented during fMRI scanning. EMG signal was amplified (CP511, Grass Technologies, West Warwick, Rhode Island, USA), filtered (band pass 30/2000 Hz), converted to digital data (Powerlab 8SP, AD Instruments, Colorado Springs, Colorado, USA), and recorded using Chart (iWorx, Dover, New Hampshire, USA) for off-line analysis. The bilateral ankle splints used during fMRI scanning were also placed during EMG collection.

Data analysis

Images were analyzed using Statistical Parametric Mapping (*http://www.fil.ion.ucl.ac.uk/spm/*). For each of the four tasks, for each participant, the first two volumes were removed because of tissue nonsaturation. For each task, remaining images were realigned, coregistered to the volumetric scan, spatially normalized, transformed into the Montreal Neurological Institute stereotaxic space, and spatially smoothed (for movement side study, 4 mm full-width at half-maximum; for movement rate study, 8 mm full-width at half-maximum). Images at rest were contrasted with images during active movement to create a contrast image for each task, for each participant.

A one-sample *t*-test was used to characterize activation during each task. One set of analyses examined the entire brain to determine the site and size of activation clusters that showed significantly increased activity during task performance, analyzed at threshold of *P* value of less than 0.001, without correction for multiple comparisons. Data analysis was performed separately for right and left brain, using first a right-brain-only mask and then a left-brain-only mask, because some right-brain and left-brain activation foci were fused in whole-brain analyses owing to midline location of foot motor areas.

A second set of analyses used a threshold-independent method to further characterize task-related fMRI changes by measuring task-related signal change in the single participant contrast images, within a 565 mm^3 mesial precentral gyrus region of interest representing leg primary motor cortex within each hemisphere, as described previously [16]. Task-related signal change within these two regions of interest was extracted from each participant's data using MarsBaR (*http://marsbar.sourceforge.net/*) [17].

A paired *t*-test was used to directly contrast, at threshold *P* value of less than 0.01, uncorrected, right versus left movement; and slow versus fast movement.

For EMG data, Chart (iWorx) was used to convert the EMG voltage measurement to a root mean square (RMS) value (which is the square root of the mean square across samples) for the first 20 s of a rest block, and of a movement block, separately for each of the tasks. Thus, for each muscle, and each task or rest state, a 20 s block of EMG activity is reduced to a single RMS value. For each of the two muscles, the ratio of (RMS during active)/(RMS during rest) was then determined for each task.

Statistical analyses used two-tailed, nonparametric methods. A laterality index was calculated for signal change data, defined as $(C-I)/(C+I)$, where C and I are leg primary motor cortex contralateral and ipsilateral to movement, respectively.

Results

All participants performed as requested during fMRI. Fast foot movements were 2.0 ± 3 Hz (mean $\pm$ SEM). Demographics are presented in Table 1.

Movement side

EMG found that the main movement was unilateral, as requested (Table 2). During left foot movement, minor but significant mirror movements in the right TA were present.

Brain activation during right foot movements was generally larger than during left foot movements (Table 3). During movement of the right (dominant) foot, activation was seen in bilateral SMC, SMA, cerebellum, and inferior

Table 1 Participant demographics

	Movement side study	Movement rate study
n	12	12
Age	42 ± 4	66 ± 4
Sex	12M	7F/5M
Handedness	$+1.9 \pm 0.1$	$+2.0 \pm 0$
Footedness	$+1.6 \pm 0.1$	$+1.2 \pm 0.2$

The handedness and footedness scores confirm that all participants were right-side dominant. Data are mean $\pm$ SEM.
F, female; M, male.

parietal lobule (IPL). Note that in all cases, SMC activation was fused with SMA activation and so is reported in this manner. Though left (nondominant) foot movement activated a similar network, activation volume was smaller within homologous structures (e.g. cerebellum ipsilateral to movement) as compared with right foot movements, in all cases except for ipsilateral IPL. Right foot movement was additionally associated with activation in left putamen and right anterior cingulate, whereas left foot movement was also associated with activation of several additional brain regions including right dorsolateral prefrontal cortex (DLPFC).

Direct comparison of the tasks using paired *t*-testing found significantly larger activation for right–left movement in the left hemisphere movement circuit, and for left–right in right hemisphere movement circuit. Consistent with above, right–left showed larger differences than left–right comparison did within SMC/SMA and cerebellum.

Analysis of task-related signal change in primary motor cortex (Table 4) identified two main findings. First, also consistent with above, and despite comparable EMG findings, right foot movement was associated with a higher degree of signal change in each motor cortex as compared with left foot movement. Second, the laterality index for primary motor cortex signal change was significantly lower during left (nondominant) foot movement, as compared with right (dominant) foot movement.

Table 2 Electromyography

Task	Movement side			Movement rate		
Muscle	Right	Left	*P*	Slow	Fast	*P*
Right TA	22.8±5.0	2.3±0.43[a]	<0.005	18.7±3.9	80.8±16.5	<0.005
Left TA	1.02±0.06	22.7±5.3	<0.005	1.6±0.6	3.2±1.4[a]	<0.005

Data (mean±SEM) for the 10 participants from whom EMG data were collected, with each cell displaying mean EMG activity during that task/muscle divided by EMG activity during rest. These participants had age 38±4 years, sex six females/four males, and were all right-footed and right-handed. The *P* values reflect two-tailed Wilcoxon rank sums test comparing the two tasks for a given muscle, separately for the 'movement side' and the 'movement rate' study. For the movement side study, the right TA was significantly more active during right movement as compared with left movement, and the left TA was significantly more active during left movement as compared with right movement. For the movement rate study, TA activity on both sides was significantly higher during the fast right movement as compared with slow right foot movement.

TA, tibialis anterior.

[a]Indicates significant mirror movements, that is, the value for (active EMG/rest EMG) in the muscle intended to be at rest was significantly ($P<0.05$) different from the null hypothesis value of 1 by two-tailed Wilcoxon signed-rank test.

Table 3 Movement side: effect on activation size

	Right foot movement	Left foot movement
Left		
SMC + SMA	1895	397
Cerebellum	556	1429
IPL	1853	551
Putamen[a]	370	
Insula		142
VL thalamus		47
DM thalamus		23
Right		
SMC + SMA	615	1319
Cerebellum	1693	109
IPL	354	176
DLPFC		39
Anterior cingulate	105	
Premotor	108	103

This table reports all sensorimotor clusters, as well as the largest clusters. Results are reported in 8 mm^3 voxels.

DM, dorsomedial; DLPFC, dorsolateral prefrontal cortex; IPL, inferior parietal lobule; SMA, supplementary motor area; SMC, sensorimotor cortex; VL, ventrolateral.

[a]Indicates a cluster that extends to insula.

Movement rate

EMG found that minor but significant ($P<0.05$) mirror movements were present in left TA during fast but not slow

Table 5 Movement rate: effect on activation size

	Slow right foot movement	Fast right foot movement
Left		
SMC + SMA	1293	1935
Cerebellum	702	3023
IPL	303	211
Insula	218	
Thalamus, posterior putamen, globus pallidus	293	
Right		
SMC + SMA	547	808
Cerebellum	824	3791
IPL	408	154
DLPFC		101
Insula	143	
Thalamus	66	
Putamen, posteriorly	59	
Cingulum	40	

Significantly activated clusters during the two rates of right foot movement. Cluster size in 8 mm^3 voxels.

DLPFC, dorsolateral prefrontal cortex; IPL, inferior parietal lobule; SMA, supplementary motor area; SMC, sensorimotor cortex.

Table 4 Task-related signal change according to side or rate of foot movement

	Movement side			Movement rate		
	Right	Left	*P*	Slow	Fast	*P*
Left MI	0.43±0.04	0.23±0.04	<0.03	0.25±0.07	0.22±0.07	0.42
Right MI	0.40±0.03	0.19±0.04	<0.01	0.23±0.07	0.20±0.09	0.83
Laterality index for MI signal	0.03±0.007	−0.12±0.03	0.001	−0.37±0.22	1.33±1.11	0.18

Mean±SEM. *P* values reflect two-tailed Wilcoxon signed-rank test comparing either right with left, or slow right with fast right, foot movement. Right, as compared with left, foot movement was associated with a significantly higher degree of signal change bilaterally. The laterality index was lower during left, as compared with right, foot movement. In the movement rate study, mean signal change in left SI was similar to left MI, being 0.23± for both tasks.

MI, primary motor cortex.

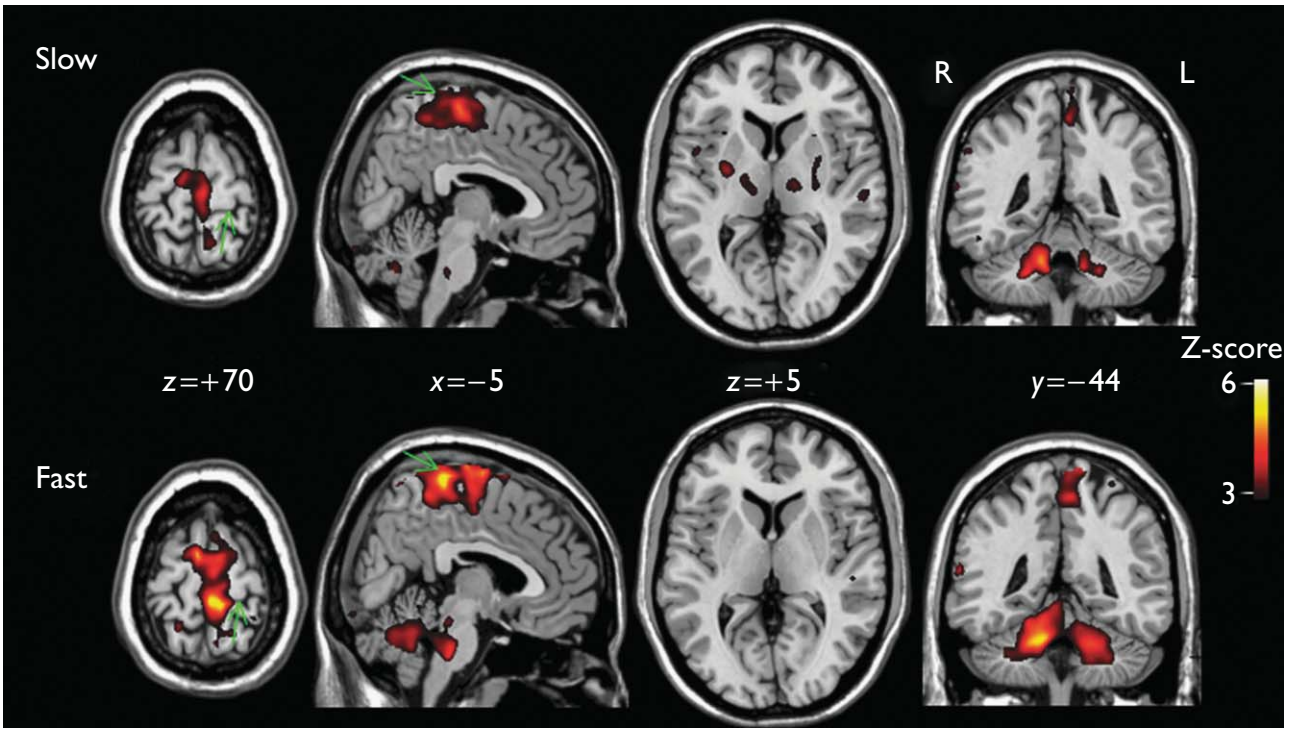

Fig. 1 Brain activation during slow and during fast movement of the right foot. In the first two columns, larger activation within left sensorimotor cortex and supplementary motor area is apparent with faster movement (green arrows indicate left central sulcus). The third column indicates that in bilateral deep gray matter, activation is present with slow, but absent with fast, movement. The fourth column demonstrates larger activation in bilateral cerebellum with fast movement. The numbers between rows indicate the Montreal Neurological Institute coordinate for the brain slice. L=left brain, R=right brain.

right foot movements, and right TA EMG activity was greater when comparing the slow with the fast right foot movement (Table 2).

Cortical and cerebellar activation during fast right foot movement was generally larger than during slow. During slow movements, activation was seen in bilateral SMC, SMA, cerebellum, IPL, insula, thalamus, and posterior putamen (Table 5). Fast movements activated a similar pattern, with a larger volume of activation in each site except that IPL activation was smaller, a new focus of right DLPFC activation was present, and deep gray matter activation was absent (Fig. 1).

Comparison of the results between the slow and fast tasks using paired *t*-testing found that activation was significantly larger during the slow task in the ventral anterior nucleus of the right thalamus. Areas significantly larger during the fast task included left SMC and bilateral cerebellum.

The magnitude of task-related signal change in left primary motor cortex (Table 4) did not significantly differ between the two right foot tasks, being 0.25 ± 0.07 for the slow movements and 0.22 ± 0.07 for the fast movements, task ($P=0.42$), and neither did the laterality index.

Discussion

To date, the cerebral processes related to control of foot movement have received limited study. This study found that movement of the right (dominant) foot, as compared with movement of the left (nondominant) foot, is associated with larger activation volume, higher amplitude of task-related signal change, and more lateralized motor cortex activation. When examining brain events in relation to speed of foot movements, the faster movement task was associated with larger activation in cerebral and cerebellar areas and smaller activation in deep gray structures. Together, these studies provide new insights, with potential clinical implications.

Movement of the dominant (right) foot showed greater activation (Tables 3 and 4) than did movement of the nondominant (left) foot, despite comparable EMG signal in the active foot across the two tasks and greater mirror movements in the right foot during left foot movement (Table 2). This is the opposite of what has been found in numerous studies examining the hand, where nondominant movements are generally associated with larger activation [8–11]. This suggests a fundamental difference in brain organization between hand and foot, perhaps reflecting the foot, more than hand, commonly participating in bilateral movements. Given that dominance-related asymmetries can be preserved after central nervous system injury such as stroke [18], this finding could have clinical significance in the design of physiotherapy protocols. Nondominant hand movements show lower hemispheric lateralization, that is, a lower laterality index, as compared with dominant hand movements. This study found that this remains true for foot movement (Table 4), consistent with an earlier study [19].

Fast movement of the dominant right foot activated larger regional brain volumes as compared with slow movements (Table 5, Fig. 1), similar to what has been described in relation to speed of movements in the hand [11–13]. This

might be related to the larger EMG signal in both TA muscles during faster movements. Curiously, bilateral deep gray matter structures showed larger activation during the slower foot movement task, in contrast to findings for the hand [20]. This suggests that slow foot movement is not simply a reduced version of faster movements, and that additional activity such as in corticostriatal circuits are invoked for slower movements, perhaps in relation to sequencing of individual lower extremity movements [21]. This finding might be useful when devising strategies to restore gait given that neurological disease generally produces a slowing of lower extremity movements. Interestingly, movements at either the faster rate or with the nondominant side were associated with increased activation in right DLPFC, an area related to executive functions and to motor learning [22], and thus (Tables 3 and 5) foot movements as well.

This study had limitations, such as fixed order of tasks, which might have contributed to an order bias, and the differing demographics and MRI settings. Overall, however, these results provide new insights into cerebral control of foot movement, which differs in several ways from control of hand movement.

Conclusion

This, combined with our earlier study [7], provides new insights into the neurobiology of foot movements in humans. Many but not all of the principles related to cerebral control of hand movement apply to foot movement. One exception is that movement of the nondominant foot shows less activation than does the dominant foot, in contrast to findings with the hand. These findings take on particular significance as fMRI measures of ankle movement can be used as a biological marker of gait training treatment effects [23–25].

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